



General

Guideline Title

Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline.

Bibliographic Source(s)

Flowers CR, Seidenfeld J, Bow EJ, Karten C, Gleason C, Hawley DK, Kuderer NM, Langston AA, Marr KA, Rolston KV, Ramsey SD. Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. J Clin Oncol. 2013 Feb 20;31(6):794-810. [307 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- [May 12, 2016 – Fluoroquinolone Antibacterial Drugs](#) : The U.S. Food and Drug Administration (FDA) is advising that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.

Recommendations

Major Recommendations

Clinical Key Question A

What interventions are appropriate to prevent infections in patients with a malignancy who have received chemotherapy in an inpatient or outpatient setting and who are, or are anticipated to become, neutropenic as outpatients?

Question A-1

How should risk of developing a febrile neutropenic episode (FNE) be assessed in such patients who are not yet febrile? What clinical characteristics identify patients who should be offered antimicrobial prophylaxis?

Because evidence to address Question A-1 was unavailable from trials limited to outpatients, the Panel considered evidence from studies on inpatients or mixed populations. The following recommendations on risk assessment (A-1a) and patient selection for antibacterial (A-1b), antifungal (A-1c), anti-*Pneumocystis* (A-1d), and antiviral (A-1e to A-1g) prophylaxis are based on the evidence summarized here and Panel members' expert opinion.

Recommendation A-1a. Risk for developing an FNE should be systematically assessed (in consultation with infectious disease specialists as needed), including patient-, cancer-, and treatment-related factors. The Panel supports the recommendations in the American Society of Clinical Oncology (ASCO) guideline on white blood cell (WBC) growth factors (Smith et al., 2006) that granulocyte colony-stimulating factor (CSF) prophylaxis be considered before the development of neutropenia for appropriate patients as defined in that guideline.

Recommendation A-1b. The Panel suggests that clinicians consider the use of antibacterial prophylaxis only for patients expected to experience profound neutropenia (defined as absolute neutrophil count [ANC] $<100/\mu\text{L}$) likely to last for ≥ 7 days. The Panel does not recommend routine antibacterial prophylaxis for patients with neutropenia that is less severe or of shorter duration. Currently, there are no chemotherapy regimens for solid tumors that would routinely be expected to produce profound neutropenia for ≥ 7 days. Therefore, the Panel does not recommend routine use of antibacterial prophylaxis for patients with solid tumors undergoing conventional chemotherapy with or without biologics such as trastuzumab, bevacizumab, or cetuximab. However, antibacterial prophylaxis might be recommended for patients at high risk of mortality if an FNE occurs.

Recommendation A-1c. The Panel recommends administering antifungal prophylaxis to decrease invasive fungal infections (IFI) resulting from opportunistic yeast or mold species to patients receiving chemotherapy expected to cause profound neutropenia (ANC $<100/\mu\text{L}$) for ≥ 7 days, which confers substantial risk ($>6\%$ to 10%) for IFI. The Panel does not recommend antifungal prophylaxis for patients with solid tumors undergoing conventional-dose chemotherapy with or without biologics such as trastuzumab, bevacizumab, or cetuximab.

Recommendation A-1d. Patients receiving chemotherapy regimens associated with a risk $>3.5\%$ for pneumonia resulting from *Pneumocystis jirovecii* (PCP; e.g., those with ≥ 20 mg of prednisone equivalents daily for ≥ 1 month or those based on purine analogs) are eligible for prophylaxis.

Recommendation A-1e. Antiviral prophylaxis should be offered to patients known to be at substantial risk for reactivation of hepatitis B virus (HBV) infection.

Recommendation A-1f. Prophylaxis to prevent reactivation of infection because of herpesviruses (herpes simplex virus [HSV] or varicella-zoster virus [VZV]) is recommended for seropositive patients undergoing therapy for certain hematologic malignancies (see Literature Review and Analysis section in the original guideline document for details).

Recommendation A-1g. Seasonal influenza immunization is recommended for all patients undergoing treatment for malignancy and for all family and household contacts.

Question A-2

What antimicrobial drug classes should be used to prevent infection in afebrile neutropenic outpatients who should be offered prophylaxis?

Because evidence was unavailable from trials limited to outpatients, the Panel considered evidence from studies on inpatients or mixed populations. Recommendations A-2a to A-2f on prophylaxis for neutropenic but afebrile outpatients, evaluated and found likely to benefit from prophylaxis as described in Recommendations A-1a to A-1g, are based on the summarized evidence and Panel members' expert opinion. Similarly, because evidence was unavailable to directly compare different durations and timing (start and stop dates) for prophylactic therapies, the suggestions of the Panel on timing and duration reflect members' experience and expert opinion.

Recommendation A-2a. The Panel recommends using antibacterial prophylaxis with an orally administered, systemically absorbed fluoroquinolone to prevent invasive infection resulting from Gram-negative bacilli in outpatients with profound neutropenia expected for ≥ 7 days in association with severe mucositis (e.g., from primary or salvage remission-induction therapy for acute leukemia, dose-intensive postremission consolidation for acute leukemia, or hematopoietic stem-cell transplantation [HSCT]). Note that prophylaxis may be less effective in environments where $>20\%$ of Gram-negative bacilli are resistant to fluoroquinolones.

Recommendation A-2b. The Panel recommends an orally administered triazole antifungal or an echinocandin parenterally administered in the outpatient setting as prophylaxis against infection with opportunistic yeasts, but only for those with profound neutropenia and mucositis expected to

last ≥ 7 days and in environments with $>10\%$ risk of invasive *Candida* infection. A mold-active triazole is recommended in environments with a substantial risk ($>6\%$) for invasive aspergillosis.

Recommendation A-2c. The Panel recommends that prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) only be used if the risk for PCP is $>3.5\%$ (e.g., patients administered regimens with ≥ 20 mg of prednisone equivalents daily for ≥ 1 month or those based on purine analogs; see Recommendation A-1d). Alternatives for patients with sulfa-based hypersensitivities are provided in the Literature Review and Analysis in the original guideline document.

Recommendation A-2d. The Panel recommends an antiviral nucleoside analog with demonstrated activity against HBV (e.g., lamivudine) as prophylaxis for those at substantial risk for reactivation of HBV infection.

Recommendation A-2e. The Panel recommends using a nucleoside analog to prevent herpesvirus infections in those at risk from the initiation of cytotoxic therapy until myeloid reconstitution.

Recommendation A-2f. Influenza immunization should use the trivalent inactivated vaccine. In select circumstances after proven exposure of a susceptible patient with cancer, a neuraminidase inhibitor (e.g., oseltamivir, zanamivir) may be offered.

Question A-3

What additional precautions are appropriate to prevent exposure of neutropenic but afebrile outpatients with a malignancy to infectious agents or organisms?

Recommendation A-3. Readers are referred to a separate ASCO guideline with recommendations on care of central venous catheters (CVC) in oncology patients (see the National Guideline Clearinghouse [NGC] summary of the ASCO guideline [Central venous catheter care for the patient with cancer: American Society of Clinical Oncology clinical practice guideline](#)). Because direct evidence was unavailable from randomized trials on many of the other measures and precautions discussed in this section, the Panel considered evidence from uncontrolled and retrospective studies. Recommendations A-3a to A-3c are based on evidence summarized in sources cited and Panel members' expert opinion.

Recommendation A-3a. All health care workers and caregivers (particularly those caring for neutropenic oncology patients) should follow hand hygiene guidelines including handwashing practices to reduce exposure through contact transmission and respiratory hygiene/cough etiquette guidelines to reduce exposure through droplet transmission and should receive annual trivalent split influenza vaccine to protect patients and themselves.

Recommendation A-3b. Outpatients with neutropenia resulting from cancer therapy should avoid prolonged contact with environments that have high concentrations of airborne fungal spores (e.g., construction and demolition sites).

Recommendation A-3c. None of the following measures are routinely necessary to prevent infection of afebrile outpatients with a malignancy and neutropenia: protected environments (high-efficiency particulate air [HEPA] filters with or without laminar air flow), respiratory masks (to prevent invasive aspergillosis), footwear exchange at entry and exit, and the neutropenic diet or similar nutritional interventions. Gowning and gloving should only be considered in accordance with local infection prevention and control practices for antibiotic-resistant organisms such as methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant enterococci, or extended-spectrum β -lactamase-producing and carbapenemase-producing Gram-negative bacilli.

Clinical Key Question B

Which patients with a malignancy and febrile neutropenia are appropriate candidates for outpatient management?

Question B-4

What clinical characteristics should be used to select patients for outpatient empiric therapy?

Recommendation B-4. Because medical complications occurred in up to 11% of patients identified as low risk for medical complications of fever and neutropenia (FN) in studies validating risk indices or scoring systems, the Panel considers inpatient treatment as the standard approach for managing an FNE. However, outpatient management may be acceptable for carefully selected patients. When considering a patient with FN for outpatient management, the Panel recommends that evaluation begin with a systematic assessment of risk for medical complications using a validated index. Of the tools available to estimate risk in adults, the Multinational Association for Supportive Care in Cancer (MASCC) risk index (see Table 3 in the original guideline document) has been evaluated most thoroughly; Talcott's rules have also been validated in prospective studies. However, if the clinician has any reservations with respect to the accuracy of an index for an individual, the FNE should be managed in the hospital even if the patient is classified as low risk (MASCC score ≥ 21 or Talcott group 4). Table 4 in the original guideline document provides a list of additional factors to take into account when assessing a given patient's risk for medical complications in the setting of outpatient management.

Patients meeting any of the criteria listed in Table 4 in the original guideline document, those with MASCC score <21, and those in Talcott groups 1 to 3 should not be managed as outpatients. Moreover, neither a currently available risk index nor the criteria in Table 4 in the original guideline document should substitute for clinical judgment when deciding whether a given patient with an FNE should be admitted to the hospital for inpatient management.

Question B-5

Should outpatients with FN at low risk for medical complications receive their initial dose(s) of empiric antimicrobial(s) in the hospital or clinic and be observed, or can some selected for outpatient management be discharged immediately after evaluation?

Recommendation B-5. The duration of observation before outpatients were discharged varied considerably among studies that directly compared inpatient versus outpatient empiric therapy or oral versus intravenous (IV) regimens in outpatients. Lacking evidence from direct comparisons, the Panel members' expert opinion agrees with other groups that physician assessment should occur soon (e.g., within 15 minutes) after triage for patients presenting with FN within 6 weeks of having received chemotherapy for a malignancy (Beveridge et al., 1999; Bullard et al., 2008; Bell et al., 2010). Although multiple studies report it can be difficult to achieve this target (Nirenberg et al., 2004; Courtney et al., 2007; Richardson et al., 2009; Okera et al., 2011), the Panel recommends that the first dose of empiric therapy be administered within 1 hour after triage from initial presentation in the clinic, emergency room, or hospital department, after fever has been documented in a neutropenic patient, and pretreatment blood samples have been drawn. The Panel also recommends that patients identified as low risk and selected for outpatient management be observed for at least 4 hours before discharge to verify they are stable and can tolerate the regimen they will receive.

Question B-6

What psychosocial and logistic requirements must be met to permit outpatient management of patients with FN?

Recommendation B-6. Direct comparative evidence was unavailable for any of these factors. On the basis of members' expert opinion, the Panel recommends that an oncology patient who develops FN during or after chemotherapy should meet each of the following criteria to receive empiric therapy as an outpatient:

- a. Residence ≤ 1 hour or ≤ 30 miles (48 km) from clinic or hospital
- b. Patient's primary care physician or treating oncologist agrees to outpatient management
- c. Able to comply with logistic requirements, including frequent clinic visits
- d. Family member or caregiver at home 24 hours a day
- e. Access to a telephone and transportation 24 hours a day
- f. No history of noncompliance with treatment protocols

Clinical Key Question C

What interventions are indicated for patients with a malignancy and febrile neutropenia who can be managed as outpatients?

Question C-7

What diagnostic procedures are recommended?

Recommendation C-7. On the basis of members' expert opinion, the Panel recommends that in the absence of an alternative explanation, fever in a patient with neutropenia from cancer therapy should be assumed to be the result of a bacterial infection. The initial diagnostic approach should maximize the chances of establishing clinical and microbiologic diagnoses that may affect antibacterial choice and prognosis. The Panel also recommends systematically evaluating the patient to identify the infectious agent and the anatomic focus (see the Literature Review and Analysis section in the original guideline document for specific details).

Question C-8

What antibacterials are recommended for outpatient empiric therapy?

Recommendation C-8. For patients with cancer, fever, and neutropenia who are at low risk for medical complications by criteria of Recommendation B-4, the Panel recommends oral empiric therapy with a fluoroquinolone (ciprofloxacin or levofloxacin) plus amoxicillin/clavulanate (or plus clindamycin for those with penicillin allergy). However, the Panel cautions against use of a fluoroquinolone as initial empiric therapy for neutropenic patients with cancer who develop fever after receiving fluoroquinolone-based antibacterial prophylaxis and in environments where the prevalence of fluoroquinolone resistance is $>20\%$. For these patients, and if deemed appropriate by the treating physician, the Panel recommends IV therapy with a regimen suitable for outpatient administration, provided they meet clinical and other criteria for outpatient management (for details, see Literature Review and Analysis in the original guideline document for Recommendations B-4 and C-9).

Hospitalized stable and responding low-risk patients receiving initial IV empiric antibacterial therapy, particularly those classified as having unexplained FN, may be considered for stepdown to an oral regimen and early discharge for outpatient follow-up and monitoring.

For patients with FN from cancer therapy who are at high risk for medical complications, the Panel recommends hospitalization for IV antimicrobial therapy and endorses the most recent (2010) recommendations from the Infectious Diseases Society of America (IDSA) (see the NGC summary of the IDSA guideline [Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America](#)).

Question C-9

What additional measures are recommended for outpatient management?

Recommendation C-9. On the basis of members' expert opinion, the Panel recommends that prudent and sensible outpatient management include:

- a. Frequent evaluation for at least 3 days, in clinic or at home
- b. Daily or frequent telephone contact thereafter to verify resolution of fever as determined by home thermometry
- c. Monitoring of ANC and platelet count for myeloid reconstitution
- d. Frequent return visits to clinic
- e. Patients should be evaluated for admission to the hospital if any of the following occur: persistent neutropenic fever (PNF) syndrome, fever recurrence, new signs or symptoms of infection, use of oral medications is no longer possible or tolerable, change in the empiric regimen or an additional antimicrobial drug becomes necessary, or microbiologic tests identify species not susceptible to initial empiric regimen.

Question C-10

How should PNF syndrome be managed?

Recommendation C-10. The Panel recommends that low-risk patients who do not defervesce after 2 to 3 days of an initial empiric broad-spectrum antibiotic regimen be re-evaluated to detect and treat a new or progressing anatomic site of infection and considered for hospitalization.

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

- Cancer
- Fever
- Neutropenia

Note: For purposes of this guideline, the Panel defined neutropenia as an absolute neutrophil count (ANC) $<1,000/\mu\text{L}$ (equivalent to $<1.0 \times 10^9/\text{L}$), severe neutropenia as ANC $<500/\mu\text{L}$ (equivalent to $<0.5 \times 10^9/\text{L}$), and profound neutropenia as ANC $<100/\mu\text{L}$ (equivalent to $<0.1 \times 10^9/\text{L}$). The Panel defined the state of being febrile as a temperature of $\geq 38.3^\circ\text{C}$ by oral or tympanic thermometry, but it did not exclude evidence from studies that used slightly different definitions (e.g., core temperature $>38^\circ\text{C}$).

Guideline Category

Evaluation

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Hematology

Infectious Diseases

Internal Medicine

Nursing

Oncology

Intended Users

Advanced Practice Nurses

Nurses

Physicians

Guideline Objective(s)

To provide guidelines on antimicrobial prophylaxis for adult neutropenic oncology outpatients and on selection and treatment as outpatients of those with fever and neutropenia

Target Population

Adults treated for malignancy who are at risk for fever and neutropenia

Interventions and Practices Considered

1. Assessment of risk for developing a febrile neutropenic episode (FNE)
2. Antibacterial (oral fluoroquinolone, trimethoprim/sulfamethoxazole [TMP-SMX]), antifungal (oral triazole or parenteral echinocandin), and antiviral (antiviral nucleoside analog, such as lamivudine) prophylaxis, as appropriate
3. Seasonal influenza immunization with trivalent inactivated vaccine
4. Precautions to prevent exposure to infectious agents
 - Central venous catheter (CVC) care
 - Hand hygiene
 - Avoidance of prolonged contact with environments that have high concentrations of airborne fungal spores
 - Gowning and gloving in accordance with local infection prevention and control practices
5. Selection of patients appropriate for outpatient management
 - Use of validated tool to assess risk for medical complications
 - Timing of initial dose of antimicrobials and discharge from hospital or clinic
 - Psychosocial and logistic requirements for outpatients
6. Outpatient management (frequent evaluation, frequent telephone contact, monitoring of absolute neutrophil count [ANC] and platelet count, frequent clinic visits, evaluation for admission to hospital)
7. Management of persistent neutropenic fever (PNF)

Major Outcomes Considered

For studies on afebrile neutropenic outpatients:

- Primary outcomes
 - Febrile episodes
 - Infections
- Secondary outcome: infection-related mortality

For studies on outpatients with fever and neutropenia (FN):

- Primary outcomes
 - Empiric treatment success
 - Overall mortality
 - Infection-related mortality
- Secondary outcomes
 - Defervescence without regimen change
 - Time to defervescence
 - Complications from infection
 - Relapsed or recurrent fever

Additional secondary outcomes relevant to both sets of studies included:

- Hospital admissions
- Duration of hospital stay
- Adverse effects of antimicrobials

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Literature Search Strategy

The MEDLINE database was searched using PubMed for relevant evidence published from 1987 through the end of April 2011. The search included terms for malignant diseases linked to terms for neutropenia, fever, or infection and to terms for clinical trials, systematic reviews, meta-analyses, or clinical guidelines. Data Supplement 1 provides the full search strategy (online at www.asco.org/guidelines/outpatientfn). One reviewer selected articles for full-copy retrieval and consulted a Panel co-chair when potential relevance was uncertain. Reference lists of articles retrieved in full copy were searched for other relevant reports. Panel members provided additional references from personal files.

Inclusion and Exclusion Criteria

Articles were selected for inclusion in the systematic review if they were fully published English-language reports on: antimicrobials for prophylaxis of infection in oncology outpatients with neutropenia from chemotherapy, development and/or validation of methods to stratify risk of complications in oncology patients with fever and neutropenia (FN), empiric antimicrobial therapy for oncology outpatients with FN, or direct comparisons of outcomes for inpatient versus outpatient management of oncology patients with FN. For clinical questions addressing antimicrobials for prophylaxis of infection or as empiric therapy for FN, study selection criteria limited inclusion to reports from randomized controlled trials (RCTs) of adult human participants, systematic reviews and meta-analyses of RCTs, or evidence-based clinical practice guidelines. Prospective or retrospective cohort studies, case-control studies, and case series were included for questions addressing risk stratification or direct comparison of inpatient

versus outpatient management. Meeting abstracts, letters, commentaries, editorials, case reports, and nonsystematic (narrative) reviews were excluded from evidence tables for all questions.

Number of Source Documents

47 articles from 43 studies met selection criteria.

Methods Used to Assess the Quality and Strength of the Evidence

Expert Consensus

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Data Extraction

For studies on afebrile neutropenic outpatients, primary outcomes included: 1) febrile episodes and 2) infections, whereas secondary outcomes included infection-related mortality. For studies on outpatients with fever and neutropenia (FN), primary outcomes included: 1) empiric treatment success (defined as recovery from FN without medical complications) and 2) overall and infection-related mortality, whereas secondary outcomes included: 1) defervescence without regimen change, 2) time to defervescence, 3) complications from infection, and 4) relapsed or recurrent fever. Additional secondary outcomes relevant to both sets of studies included: 1) hospital admissions, 2) duration of hospital stay, and 3) adverse effects of antimicrobials. Data were extracted directly into evidence tables (see Data Supplement Tables DS-3 to DS-9; online at www.asco.org/guidelines/outpatientfn) by one reviewer and checked for accuracy by a second reviewer. Disagreements were resolved by discussion and by consultation with Panel co-chairs if necessary.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Panel Composition

The American Society of Clinical Oncology Clinical Practice Guidelines Committee (ASCO CPGC) convened an Expert Panel (hereafter referred to as the Panel) consisting of experts in clinical medicine and research methods relevant to prevention and treatment of infection in patients with neutropenia after therapy for a malignancy and reflecting the perspectives of academic and private practice clinicians. The experts' fields included medical oncology, hematology, infectious diseases, oncology nursing, health services research, epidemiology, public health, and biostatistics. The Panel also included a patient representative.

Guideline Development Process

The entire Panel met once to review results of the systematic review; additional work to revise the clinical questions and to draft guideline recommendations and a manuscript was completed by telephone conferences (when necessary) and electronic review of documents.

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

All members of the Panel participated in preparation and revision of the draft guideline document and approved the final version submitted for peer review and publication in *Journal of Clinical Oncology*. Additional feedback was solicited from external reviewers. The content of the guidelines and manuscript were reviewed and approved by the American Society of Clinical Oncology Clinical Practice Guidelines Committee (ASCO CPGC) before publication.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Bell MS, Scullin P, McParlin D, et al. Neutropenic sepsis guideline. Belfast (Ireland): Northern Ireland Cancer Network; 2010.

Beveridge R, Clarke B, Janes L, et al. The Canadian Emergency Department Triage and Acuity Scale (CTAS): Implementation guidelines. *CJEM*. 1999;1(suppl 3):S1-28.

Bullard MJ, Unger B, Spence J, Grafstein E, CTAS National Working Group. Revisions to the Canadian Emergency Department Triage and Acuity Scale (CTAS) adult guidelines. *CJEM*. 2008 Mar;10(2):136-51. [PubMed](#)

Courtney DM, Aldeen AZ, Gorman SM, Handler JA, Trifilio SM, Parada JP, Yarnold PR, Bennett CL. Cancer-associated neutropenic fever: clinical outcome and economic costs of emergency department care. *Oncologist*. 2007 Aug;12(8):1019-26. [PubMed](#)

Nirenberg A, Mulhearn L, Lin S, Larson E. Emergency department waiting times for patients with cancer with febrile neutropenia: a pilot study. *Oncol Nurs Forum*. 2004 Jul;31(4):711-5. [PubMed](#)

Okera M, Chan S, Dernede U, Larkin J, Popat S, Gilbert D, Jones L, Osuji N, Sykes H, Oakley C, Pickering L, Loftis F, Chowdhury S. A prospective study of chemotherapy-induced febrile neutropenia in the South West London Cancer Network. Interpretation of study results in light of NCAG/NCEPOD findings. *Br J Cancer*. 2011 Feb 1;104(3):407-12. [PubMed](#)

Richardson S, Pallot D, Hughes T, Littlewood T. Improving management of neutropenic sepsis in the emergency department. *Br J Haematol*. 2009 Feb;144(4):617-8. [PubMed](#)

Smith TJ, Khatcheressian J, Lyman GH, Ozer H, Armitage JO, Balducci L, Bennett CL, Cantor SB, Crawford J, Cross SJ, Demetri G, Desch CE, Pizzo PA, Schiffer CA, Schwartzberg L, Somerfield MR, Sonlo G, Wade JC, Wade JL, Winn RJ, Wozniak AJ, Wolff AC. 2006 update of recommendations for the use of white blood cell growth factors: an evidence-based clinical practice guideline. *J Clin Oncol*. 2006 Jul 1;24(19):3187-205. [128 references] [PubMed](#)

Type of Evidence Supporting the Recommendations

The type of evidence supporting the recommendations is not specifically stated.

Refer to the "Literature Review and Analysis" sections of the original guideline document for specific evidence for each recommendation.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of fever and neutropenia (FN)

Potential Harms

Adverse effects of antimicrobial prophylaxis, including rash, gastrointestinal effects, and antibacterial resistance

Contraindications

Contraindications

- *Oral empiric therapy with fluoroquinolone (ciprofloxacin or levofloxacin) plus amoxicillin/clavulanate (or plus clindamycin):* Oral regimens are contraindicated for patients presenting with nausea and/or vomiting or who are otherwise unable to tolerate or absorb oral medications.
- *Outpatient management:* Patients meeting any of the criteria listed in Table 4 in the original guideline document, those with Multinational Association for Supportive Care in Cancer (MASCC) score ≤ 2 , and those in Talcott groups 1 to 3 should not be managed as outpatients.

Qualifying Statements

Qualifying Statements

Guideline Policy

The practice guideline is not intended to substitute for the independent professional judgment of the treating physician. Practice guidelines do not account for individual variation among patients and may not reflect the most recent evidence. This guideline does not recommend any particular product or course of medical treatment. Use of the practice guideline is voluntary.

Limitations of the Research and Future Directions

The American Society of Clinical Oncology (ASCO) believes that cancer clinical trials are vital to inform medical decisions and improve cancer care and that all patients should have the opportunity to participate. One major limitation of the evidence available to inform this guideline is the absence of data from randomized controlled trials (RCTs) that either studied the net effect on health outcomes or compared the efficacy and safety of alternative regimens for antibacterial prophylaxis specifically in afebrile neutropenic outpatients. Another is the lack of well-validated scales or models to assess and stratify risk for complications and mortality and thus identify afebrile outpatients with neutropenia most likely to benefit from

prophylactic antibiotics. The Panel sees a need for future research to fill these gaps.

See the original guideline document for a more detailed discussion of the limitations of the research.

Implementation of the Guideline

Description of Implementation Strategy

For information on the American Society for Clinical Oncology (ASCO) implementation strategy, please see the [ASCO Web site](#)

Implementation Tools

Foreign Language Translations

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Slide Presentation

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Flowers CR, Seidenfeld J, Bow EJ, Karten C, Gleason C, Hawley DK, Kuderer NM, Langston AA, Marr KA, Rolston KV, Ramsey SD. Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol*. 2013 Feb 20;31(6):794-810. [307 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2013 Feb 20

Guideline Developer(s)

American Society of Clinical Oncology - Medical Specialty Society

Source(s) of Funding

American Society of Clinical Oncology

Guideline Committee

Expert Panel

Composition of Group That Authored the Guideline

Panel Members: Christopher R. Flowers, MD, MS (*Co-chair*), Emory University School of Medicine, Atlanta, GA; Scott D. Ramsey, MD, PhD (*Co-chair*), Fred Hutchinson Cancer Research Center, Seattle, WA; Jerome Seidenfeld, American Society of Clinical Oncology, Alexandria, VA; Eric J. Bow, MD, CancerCare Manitoba and University of Manitoba, Winnipeg, Manitoba, Canada; Clare Karten, MS, Leukemia and Lymphoma Society, White Plains, NY; Charise Gleason, ARNP, Emory University School of Medicine, Atlanta, GA; Douglas K. Hawley, MD, One Heme Care, Cincinnati, OH; Nicole M. Kuderer, MD, Duke University Comprehensive Cancer Center, Durham, NC; Amelia A. Langston, MD, Emory University School of Medicine, Atlanta, GA; Kieren A. Marr, MD, Johns Hopkins School of Medicine, Baltimore, MD; Kenneth V.I. Rolston, MD, University of Texas MD Anderson Cancer Center, Houston, TX

Financial Disclosures/Conflicts of Interest

The Expert Panel was assembled in accordance with the American Society of Clinical Oncology (ASCO) Conflict of Interest Management Procedures for Clinical Practice Guidelines (summarized at <http://www.asco.org/guidelinescoi>). Members of the Panel completed the ASCO disclosure form, which requires disclosure of financial and other interests that are relevant to the subject matter of the guideline, including relationships with commercial entities that are reasonably likely to experience direct regulatory or commercial impact as the result of promulgation of the guideline. Categories for disclosure include employment relationships, consulting arrangements, stock ownership, honoraria, research funding, and expert testimony. In accordance with the Procedures, the majority of the members of the Panel did not disclose any such relationships.

The author(s) indicated no potential conflicts of interest.

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the [American Society of Clinical Oncology \(ASCO\) Web site](#) .

Availability of Companion Documents

The following are available:

- Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. Executive summary. J Clin Oncol 31. Electronic copies: Available in Portable Document Format (PDF) from the [Journal of Clinical Oncology Web site](#) .
- Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. Data supplement. Alexandria (VA): American Society of Clinical Oncology; 2013. 44 p. Electronic copies: Available in PDF from the [American Society of Clinical Oncology \(ASCO\) Web site](#) .
- Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. Slide set. Alexandria (VA): American Society of Clinical Oncology; 2013. 28 p. Electronic copies: Available in [PDF](#) and [PowerPoint format](#) from the ASCO Web site.
- Flowers CR, Kartern C. Communicating safe outpatient management of fever and neutropenia. J Oncol Pract. 2013 Jan 15. Electronic copies: Available from the [Journal of Oncology Practice Web site](#) .
- Understanding ASCO's recommendations for managing febrile neutropenia, with Christopher Flowers, MD. Podcast. Alexandria (VA): American Society of Clinical Oncology; 2013. Available from the [Cancer.net Web site](#) .

Patient Resources

The following is available:

- Neutropenia. Alexandria (VA): American Society of Clinical Oncology; 2012 Apr. Electronic copies: Available in [English](#) and [Spanish](#) from the Cancer.net Web site.

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